DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

94375d

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

OCT 27 2003

WARNING LETTER

VIA FEDERAL EXPRESS

Richard B. North, M.D.
President
Stimsoft, Incorporated
1000 Century Plaza, Suite 313
10630 Little Patuxent Parkway
Columbia, Maryland 21044

Dear Dr. North:

The purpose of this letter is to advise you of the objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at Stimsoft, Inc., and to request your prompt corrective action. Ms. Stephanie L. Shapley of the FDA Baltimore District Office and Ms. Barbara A. Crowl of FDA's Center for Devices and Radiological Health conducted the inspection at your site on April 22-30, 2003.

The purpose of the inspection was to determine if your activities as the sponsor of the clinical study entitled [redacted] and as the applicant of the marketing application entitled [redacted] (PMA [redacted], complied with Federal regulations. You conducted the study under an abbreviated Investigational Device Exemption and submitted the marketing application. The [redacted] is a device as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 321(h).

The inspection was conducted under a program designed to ensure that data and information contained in Investigational Device Exemption (IDE), Premarket Approval Application (PMA), and Premarket Notification [510(k)] submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the Baltimore District Office revealed violations of the requirements of Title 21, Code of Federal Regulations (21 CFR) Part 812 – Investigational Device Exemptions and Part 54 – Financial Disclosure by Clinical Investigators. At the conclusion of the inspection, Ms. Shapley and Ms. Crowl listed their findings on a Form FDA-483 "Inspectional Observations," and discussed these findings with you. The violations noted on the FDA-483 and our subsequent reviews of the inspection reports are summarized below.

1. Failure to ensure proper monitoring of the investigation (21 CFR 812.2(b)(1)(iv), 21 CFR 812.40, and 21 CFR 812.46)

Sponsors must monitor studies at adequate intervals to assure that investigators are complying with the signed agreement, investigational plan, and all applicable FDA regulations. According to procedures outlined in your PMA Amendment dated January 9, 2003, Item [redacted] the Stimsoft Clinical Affairs Manager should manage the clinical investigation according to the signed investigator agreement and investigational plan. However, there were no monitoring logs or other documentation reflecting that visits were made to the clinical sites by any Stimsoft employee, including by Stimsoft Clinical Affairs Manager, [redacted]

2. Failure to promptly secure compliance from or terminate participation by a non-compliant investigator (21 CFR 812.2(b)(1)(iv), 21 CFR 812.46 (a))

FDA regulations at 21 CFR 812.2(b)(1)(iv) and 21 CFR 812.46 (a) require a sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA, to promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. During the inspection, FDA inspectors observed various noncompliances that should have been discovered by your firm through proper monitoring. The noncompliances found include but are not limited to the following:

The study protocol was not followed. The [redacted] and [redacted] was not maintained through both the manual and [redacted] testing for two subjects. One subject had an established [redacted] outside of the investigational plan tolerable limit. Five subjects had an established [redacted] outside of the investigational plan tolerable limit. Two subjects were not maintained at the same [redacted] and [redacted] value for both manual testing and [redacted] testing.

Study forms were not completed according to the clinical investigation plan. FDA inspectors reviewed 24 of 44 case histories for completeness. Eighteen of 24 case histories reviewed contained incomplete [redacted] Adjustment Records. Three of the 24 case histories reviewed contained incomplete [redacted] Clinical Trial Session Assessments.

3. Failure to ensure that clinical investigators obtain and document informed consent and maintain records relating to the clinical investigation (21 CFR 812.2(b)(1)(iii) and 21 CFR 812.2(b)(1)(vi))

Under 21 CFR 812.2(b)(1)(iii) and (vi), sponsors are responsible for ensuring that clinical investigators obtain informed consent, maintain records, and file reports relating to the clinical investigation.

FDA inspected the principal investigator at Site [redacted] on May 27, 30, June 3, and 10, 2003. At this site, the FDA investigator noted that subject [redacted] did not consent before

treatment with investigational device. Subject [redacted] consented (signed) the informed consent document on December 6, 2001, a day before the clinical investigator and the witness completed (signed) the consent form on December 7, 2001. There was no documentation available to indicate the subjects participating in the study received a copy of their signed consent forms.

FDA inspected the principal investigator at Site [redacted] on May 9, 2003. At this site, there were no case histories of subjects who participated in the study, no copies of informed consents signed by those subjects, and no documentation of IRB approval. There is no documentation available to indicate the subjects participating in the study received a copy of their signed consent forms.

4. Failure to prepare and submit required reports (21 CFR 812.2(b)(1)(v), 21 CFR 812.150(b))

FDA regulations require sponsors to prepare and submit progress reports at regular intervals and, at least, yearly, to all reviewing IRBs (21 CFR 812.150(b)(5)). In addition, sponsors must submit a final report to the reviewing IRBs within six months after termination or completion of the investigation (21 CFR 812.150(b)(7)).

You failed to prepare and submit any progress reports during the investigation to the reviewing IRBs. You also failed to prepare and submit a final report to the IRBs within six months of completion or termination of the clinical investigation. According to your [redacted] dated January 9, 2003, the clinical investigation [redacted], also known as [redacted] ended at [redacted] y, on October 23, 2001; and at [redacted] ended on December 7, 2001. The [redacted] indicates the termination of the [redacted] also known as [redacted] at [redacted] on January 25, 2002 and at the [redacted] on January 4, 2002.

5. Failure to keep records on investigator financial disclosure (21 CFR 814.20(b)(12), 21 CFR 54.6)

You submitted a marketing application containing data from the clinical study of [redacted] including the financial disclosure documents required at 21 CFR 814.20(b)(12). As an applicant, you are required by FDA regulations at 21 CFR 54.6(a) to keep on file certain information concerning the financial interests of the clinical investigators who conducted the study, including complete records showing: any financial interest or arrangement as described in 21 CFR 54.4(a)(3)(ii); significant payments of other sorts paid to the clinical investigators by the sponsor; and any financial interests held by clinical investigators as set forth in 21 CFR 54.4(a)(3)(iv). During the inspection, however, you were not able to produce these records.

The above-described deviations are not intended to be an all-inclusive list of violations that may exist in these clinical studies. It is your responsibility as a sponsor to ensure adherence to each requirement of the Act and all applicable federal regulations.

Please advise this office, in writing, within 15 working days after receiving this letter, of the specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations. Any corrective action plan you submit must include timeframes for completion of corrective actions and copies of any agreements with, and the qualifications of, any third-party auditors or contractors you may choose to use.

Please send all requested information to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kevin M. Hopson, Consumer Safety Officer. Failure to respond to this letter and take appropriate corrective action could result in enforcement action without further notice.

A copy of this letter has been sent to the Food and Drug Administration, Baltimore District Office, 6000 Metro Drive, Suite 101, Baltimore, Maryland 21215. We request that you also send a copy of your response to that office.

If you have any questions or require additional time to respond, please call Mr. Hopson at (301) 594-4720, extension 128.

Sincerely yours,

Michael E. Marcarelli

for Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices
and Radiological Health

cc: Purged Copies:

[redacted]